M.Sc-ZOOLOGY: Semester-I: Paper-IV:

GENETICS AND EVOLUTION

UNIT-1

1.1 INTERACTION OF GENES:

Definition of Gene Interaction:

A gene interaction is an interplay between multiple genes that has an impact on the expression of an organism's phenotype. While the expression of physical traits is often described as the result of inheriting two genes, one at each allele from each parent, it is actually much more complicated.

Groups of genes interact with each other, explaining why phenotypes are so variable between individual members of a species. Understanding gene interactions is an important aspect of understanding inheritance, particularly inheritance of deleterious traits

.

Gene interactions can result in the alteration or suppression of a phenotype. This can occur when an organism inherits two different dominant genes, for example, resulting in incomplete

dominance. This is commonly seen in flowers, where breeding two flowers that pass down dominant genes can result in a flower of an unusual color caused by incomplete dominance. If red and white are dominant, for example, the offspring might be pinkish or striped in color as the result of a gene interaction.

Types of Gene Interactions

Gene interactions can be classified as

- Allelic gene interaction

- Non-allelic gene interaction

Non-allelic gene interaction

Expression of character is produced by interaction between two or more genes. The interactions we have listed below, as inter and intra allelic are of this type.

- Inter-allelic

- Intra-allelic

Inter-allelic

- Without modification of normal F2 ratio

- With modification of normal F2 ratio

Such kinds of interactions modify the normal F2 ratio (9:3:3:1). Various types of such interactions are as below.

Gene Interaction

F2 Ratio Test Cross Ratio

Complementary Gene Interaction 9:7

1:3

Supplementary Gene Interaction 9:3:4

1:1:2

Epistasis

12:3:1 2:1:1

Duplicate Factor

15:1

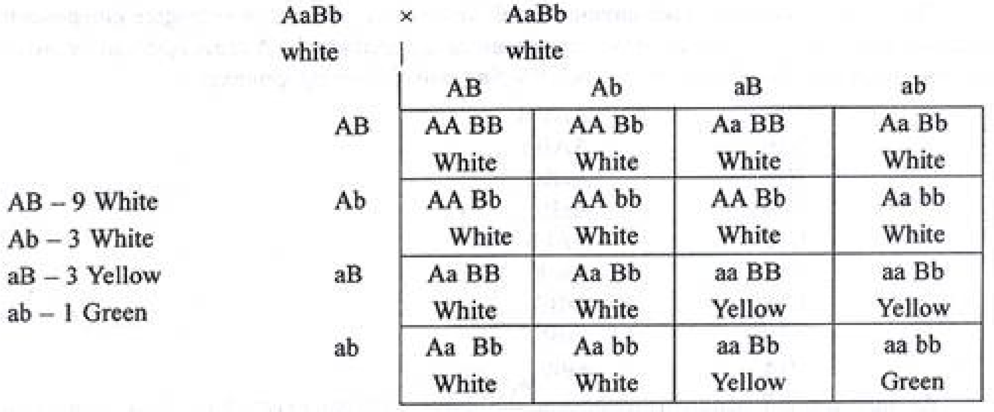
3:1

Inhibitory Factor

13:3

1:3

1



AaBb × AaBb

white white

	AB	Ab	aB	ab
AB	AA BB White	AA Bb White	Aa BB White	Aa Bb White
Ab	AA Bb White	AA bb White	AA Bb White	Aa bb White
aB	Aa BB White	Aa Bb White	aa BB Yellow	aa Bb Yellow
ab	Aa Bb White	Aa bb White	aa Bb Yellow	aa bb Green

AB – 9 White
Ab – 3 White
aB – 3 Yellow
ab – 1 Green

Polymerism or Additive Factor

9:6:1

1:2:1

1.1.1 Epistasis

Epistasis is an interaction at the phenotypic level of organization. The genes that are involved in a specific epistatic interaction may still show independent assortment at the genotypic level. In such cases, however, the phenotypic ratios may appear to deviate from those expected with independent assortment.

The epistasis is in between two genes, that is at least a dihybrid and the phenotypes are less than 4.

(a) Dominant epistasis (12: 3: 1):

When dominant allele ‘A’ masks the expression of ‘B’ ‘A’ is epistatic gene of ‘B’. A can express itself only in the presence of ‘B’ or b allele. Therefore it is called dominant epistasis. B expresses only when ‘aa’ is present. Therefore, in 9: 3: 3: 1 ratio both 9 and 3 are expressing the ‘A’ gene the ratio is now 12: 3: 1.

Example:

Complete dominance at both gene pairs, but one gene, when dominant, epistatic to the other.

Fruit colour in summer squash:

Gene pair A: White dominant to colour 12/16 white

Gene pair ‘B’ – Yellow dominant to green 3/16 yellow

Green – 1/16 both recessive aabb

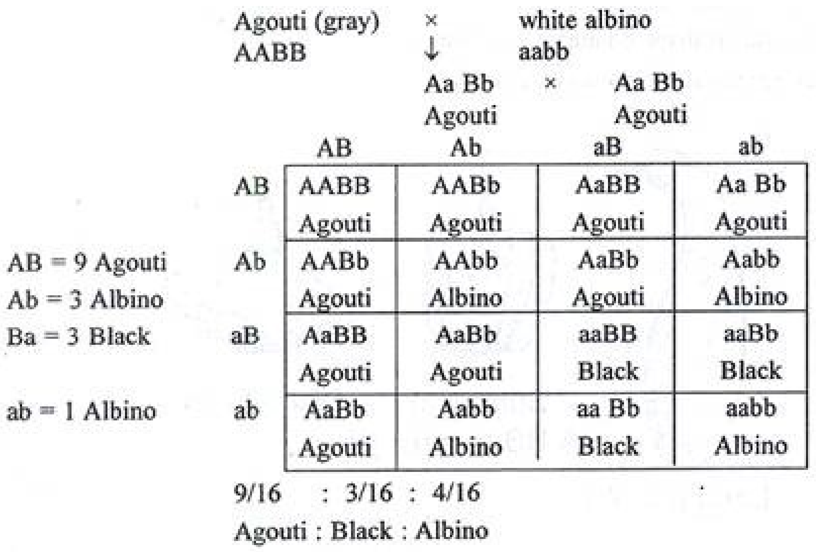
Dominant white hides the effect of yellow or green.

(b) Recessive epistasis (9:3:4):

Recessive alleles at one locus (aa) mask the phenotypic expression of other gene locus (BB, Bb or bb) such epistasis is called recessive epistasis. The alleles of ‘B’ locus express themselves only when epistatic locus ‘A’ has dominant allele like AA or Aa. The phenotypic ratio is 9: 3: 4.

Example:

Complete dominance at both gene pairs, but one gene, when homozygous recessive, is epistatic to the other.

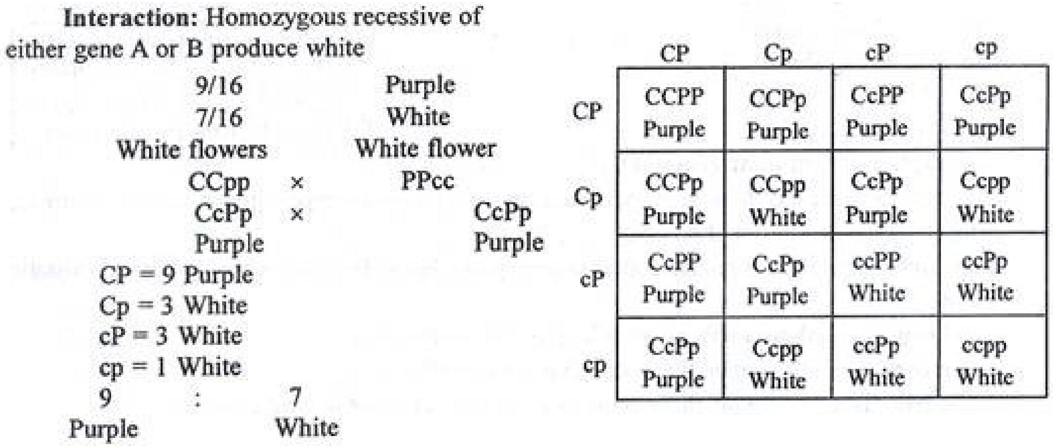


Agouti (gray) × white albino
AABB ↓ aabb
Aa Bb × Aa Bb
Agouti Agouti

	AB	Ab	aB	ab
AB	AABB Agouti	AABb Agouti	AaBB Agouti	Aa Bb Agouti
Ab	AABb Agouti	AAbb Albino	AaBb Agouti	Aabb Albino
aB	AaBB Agouti	AaBb Agouti	aaBB Black	aaBb Black
ab	AaBb Agouti	Aabb Albino	aa Bb Black	aabb Albino

AB = 9 Agouti
Ab = 3 Albino
Ba = 3 Black
ab = 1 Albino

9/16 : 3/16 : 4/16
Agouti : Black : Albino



Interaction: Homozygous recessive of either gene A or B produce white

9/16 Purple
7/16 White
White flowers White flower
CCpp × PPcc
CcPp × CcPp
Purple Purple
CP = 9 Purple
Cp = 3 White
cP = 3 White
cp = 1 White
9 : 7
Purple White

	CP	Cp	cP	cp
CP	CCPP Purple	CCPp Purple	CcPP Purple	CcPp Purple
Cp	CCPp Purple	CCpp White	CcPp Purple	Ccpp White
cP	CcPP Purple	CcPp Purple	ccPP White	ccPp White
cp	CcPp Purple	Ccpp White	ccPp White	ccpp White

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In Mouse coat colour.

Gene pair A: colour dominant over albino.

Gene pair ‘B’ agouti colour dominant over black.

Interaction: homozygous albino is epistatic to aguoti and black.

Agouti 9/16

Black 3/16

Albino 4/16

(c) Duplicate recessive gene (9: 7):

If both gene loci have homozygous recessive alleles and both of them produce identical phenotype the F2 ratio 9:3:3:1 would be 9:7. The genotype aaBB, aaBb, AAbb, Aabb and aabb produce same phenotype. Both dominant alleles when are present together only then they can complement each other. This is known as complementary gene.

Examples:

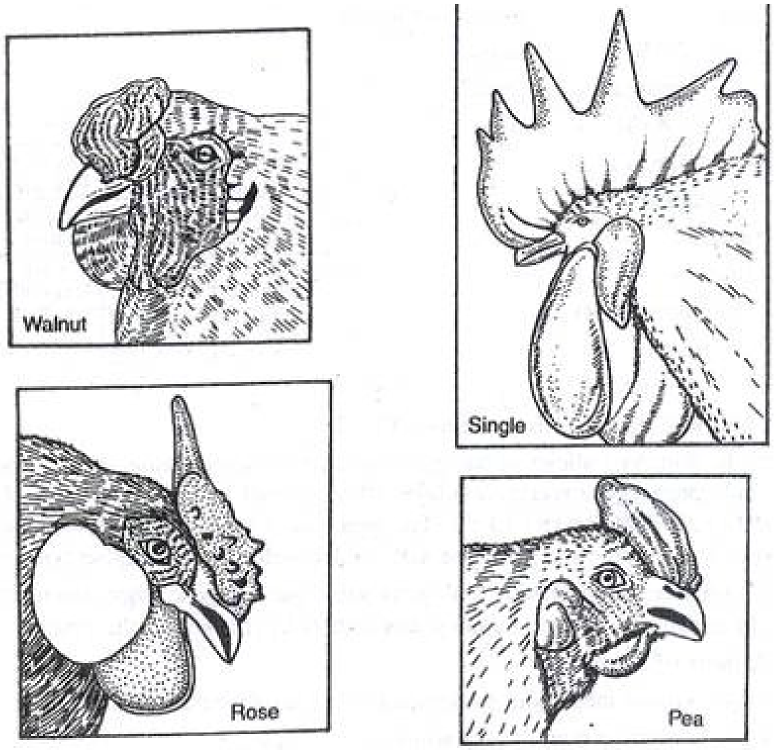
Complete dominance at both gene pairs, but either recessive homozygote is epistatic to the effect of the other gene.

In sweet pea flower colour:

Gene pair ‘A’ – Purple dominant over white.

Gene pair ‘B’ – Colour dominant over colourless (white).

3



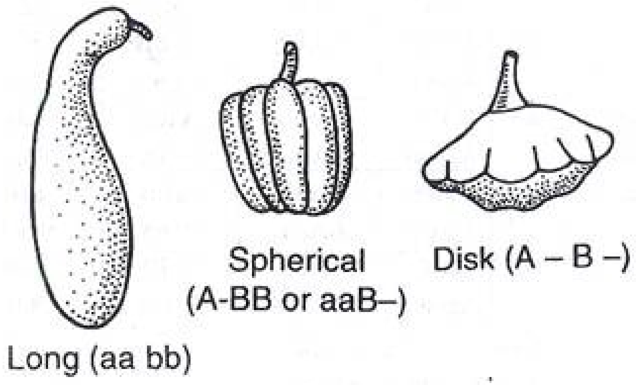


Fig. 39.1. Shape of summer squash.

(d) Duplicate genes with cumulative effect (9:6:1):

Certain phenotypic traits depend on the dominant alleles of two gene loci. When dominant is present it will show its phenotype. The ratio will be 9: 6: 1.

Example:

Complete dominance at both gene pairs, interaction between both dominance to give new phenotypes.

Fruit shape in summer squash

Gene pair ‘A’ sphere shape dominant over long.

Gene pair ‘B’ sphere shape dominant overlong.

Non epistatic Inter allelic genetic interaction:

In some cases two pairs of genes determine same phenotype but assorted independently, produce new phenotypes by mutual epistatic interaction. The F2 ratio remains the same as 9:3:3:1.

Example:

Each gene pair affecting the same character

complete dominance at both gene pairs, new

phenotypes resulting from interaction

between dominants, and also from interaction

between both homozygous recessives.

Fig: Various types of combs in cock

Gene Pair A: Rose comb dominant over non

rose.

Gene Pair B: Pea comb dominant over non

pea.

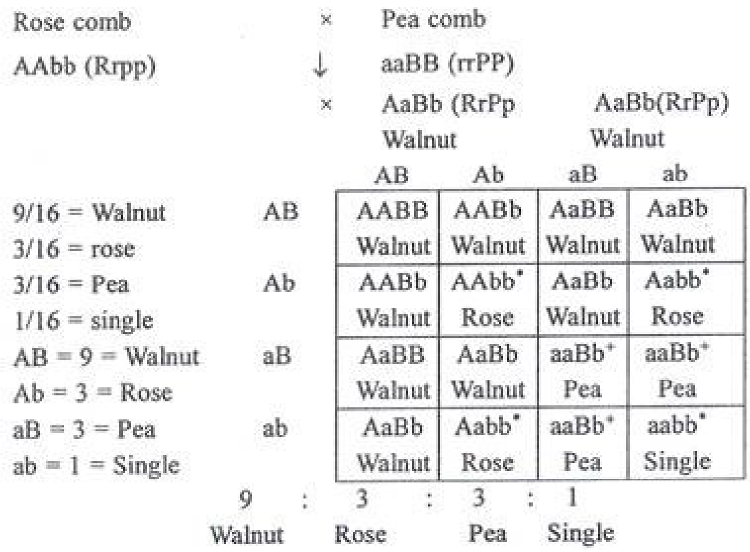
Interaction:

Dominant of rose and pea produce walnut

comb. Homozygous recessive for rose and

pea produce single comb.

4



Rose comb × Pea comb

AAbb (Rrpp) ↓ aaBB (rrPP)

× AaBb (RrPp AaBb(RrPp)

Walnut Walnut

9/16 = Walnut
3/16 = rose
3/16 = Pea
1/16 = single
AB = 9 = Walnut
Ab = 3 = Rose
aB = 3 = Pea
ab = 1 = Single

	AB	Ab	aB	ab
AB	AABB Walnut	AABb Walnut	AaBB Walnut	AaBb Walnut
Ab	AABb Walnut	$AAbb^*$ Rose	AaBb Walnut	$Aabb^*$ Rose
aB	AaBB Walnut	AaBb Walnut	$aaBb^+$ Pea	$aaBb^+$ Pea
ab	AaBb Walnut	$Aabb^*$ Rose	$aaBb^+$ Pea	$aabb^*$ Single

9 : 3 : 3 : 1

Walnut Rose Pea Single

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According to Bateson and Punnett such result is obtained because by combination of homozygous recessive genes (bb) and a homozygous or heterozygous dominant AA or Aa the Rose comb is produced; and by combination of homozygous recessive (aa) and homozygous or heterozygous dominant condition BB or Bb produce pea comb while the single type comb is produced by double recessive aabb genes. ‘A’ gene determines the shape of rose comb and ‘B’ gene determines the shape of Pea comb, but when both genes combine a new shape Walnut appears. In the cross between two types of Walnut chickens 4 phenotypes appear. The genes here do not determine themselves in the development of character but modify the character determined by a basic gene. These genes are called supplementary or modifying genes.

1.1.2 Genes & Environment

Gene–environment interaction (or **genotype–environment interaction** or **G×E**) is the phenotypic effect of interactions between genes and the environment.Gene–environment interaction is exploited by plant and animal breeders to benefit agriculture. For example, plants can be bred to have tolerance for specific environments, such as high or low water availability.

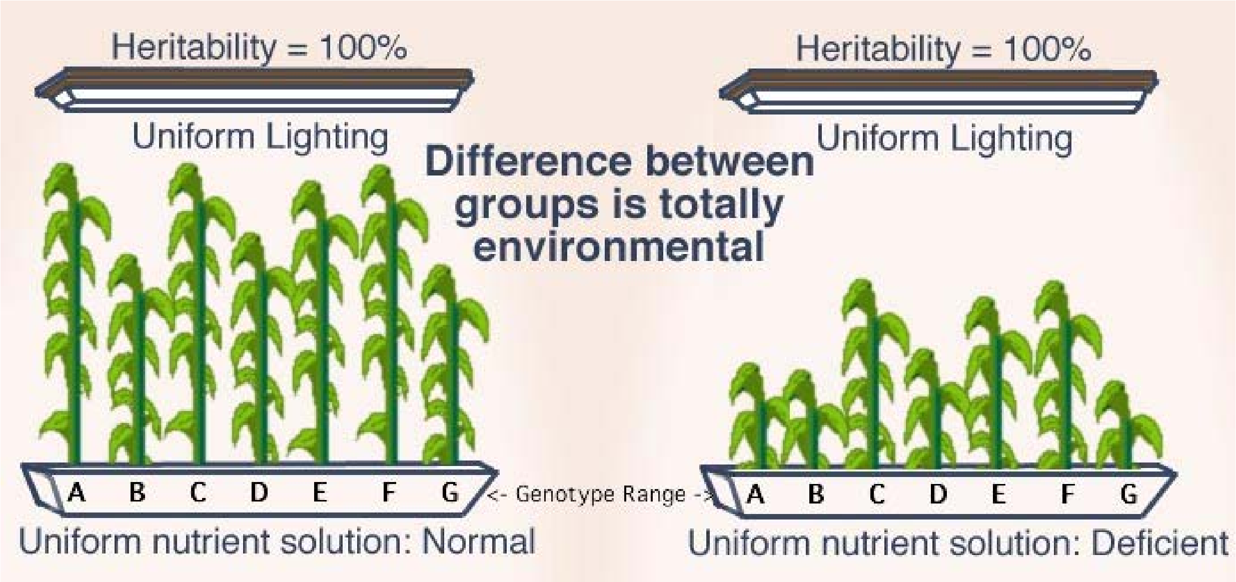
The way that trait expression varies across a range of environments for a given genotype is called its norm of reaction.

Developmental gene–environment interaction is a concept more commonly used by

developmental geneticists and developmental psychobiologists. Developmental interaction is not seen merely as a statistical phenomenon. Whether statistical interaction is present or not, developmental interaction is in any case manifested in the causal interaction of genes and environments in producing an individual's phenotype.

Example-1:

A classic example of gene–environment interaction is Cooper and Zubek's experiment on maze-running ability in rats. They produced a remarkable difference in maze running ability in two selected lines after seven generations of selecting "bright" and "dull" lines by breeding the best and worst maze running rats with others of similar abilities. The difference between these lines was clearly genetic since offspring of the two lines, raised under identical typical lab conditions, performed differently. This difference disappeared in a single generation, if those rats were raised in an enriched environment with more objects to explore and more social interaction. [8] This result suggests that maze running ability is the product of a gene-by-environment interaction; the genetic effect is only seen under some environmental conditions. However, Cooper and Zubek warned against overinterpreting the results due to a potentially problematic ceiling effect in the maze running task used. Sesardic has noted that the study has never been replicated.


Heritability = 100%
Uniform Lighting
Heritability = 100%
Uniform Lighting
Difference between groups is totally environmental
A B C D E F G
<- Genotype Range ->
A B C D E F G
Uniform nutrient solution: Normal
Uniform nutrient solution: Deficient

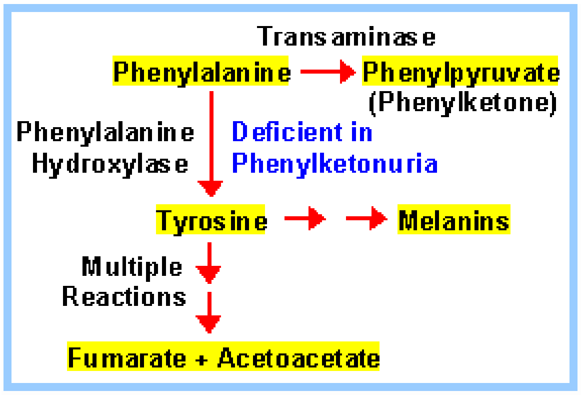

Transaminase
Phenylalanine
Phenylpyruvate (Phenylketone)
Phenylalanine Hydroxylase
Deficient in Phenylketonuria
Tyrosine
Melanins
Multiple Reactions
Fumarate + Acetoacetate

Figure: *In some combinations of environments and genotypic ranges, heritability can be 100%*

even while group differences are completely environmental. For heritability to be 100%, random variation in expression must not occur

Example-2:

Phenylketonuria (PKU) is a human genetic condition caused by mutations to a gene coding for a particular liver enzyme. In the absence of this enzyme, an amino acid known as phenylalanine does not get converted into the next amino acid in a biochemical pathway, and therefore too much phenylalanine passes into the blood and other tissues. This disturbs brain development leading to mental retardation

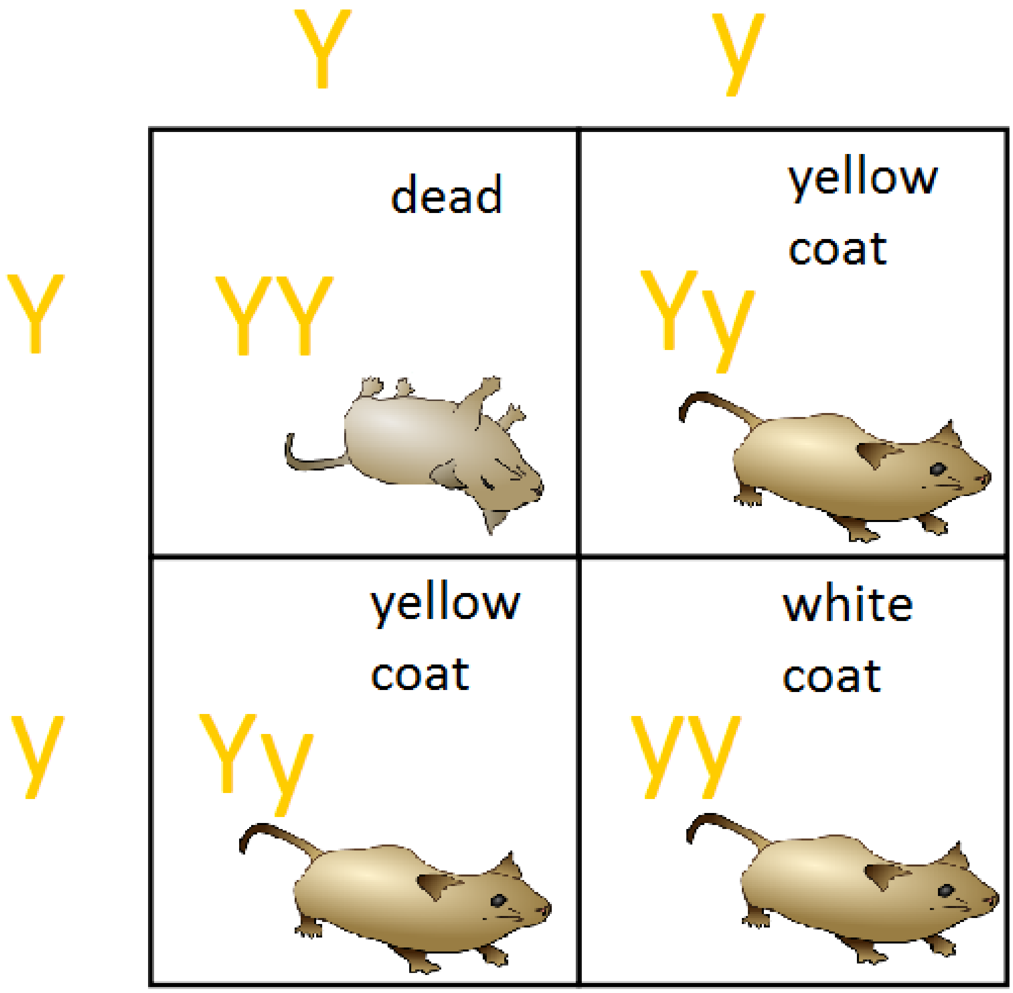
and other problems. PKU affects approximately 1 out of every 15,000 infants in the U.S. However, most affected infants do not grow up impaired because of a standard screening program used in the U.S. and other industrialized societies. Newborns found to have high levels of phenylalanine in their blood can be put on a special, phenylalanine-free diet. If they are put on this diet right away and stay on it, these children avoid the severe effects of PKU.

Fig: Phenylketonuria

1.1.3 Lethality

Genes which result in viability reduction of individual or become a cause for death of individuals carrying them are called as lethal genes. Phenomenon of action of lethal genes is called as **lethality**.

Some lethal genes cause death of zygote or the early embryonic stage while some express their effect in later stages of development. Individuals carrying dominant lethal will die. Even though the dominant lethal is eliminated from the genotype of population previously carrying it, the 6



recessive lethals are still carried in heterozygous condition. The recessive lethal in heterozygous condition reduce the viability and when they occur in homozygous condition produce lethal effect.

Usually lethal genes are dominant with respect to the phenotype they control and recessive for their lethal actions.

Example of Lethal Genes

In case of **mice** (By Cuenot)

In a cross of a yellow mouse with another yellow, yellow and brown mice are obtained in 2:1

ratio. True breeding yellow mice never obtained. In 1917, Stiegseder reported that 1/4th of the offspring die in embryonic condition in such crosses. These premature dead forms are dominant

homozygous.

According to Cuenot gene Y has multiple effects. It controls the yellow color of the body and affects to individual viability. It means the gene is dominant for body color and recessive with respect to lethality. The living yellow forms are heterozygous and somehow manage to survive.

Lethal genes were first discovered by Lucien Cuénot while studying the inheritance of coat colour gene in mice. He expected a phenotype ratio from a heterozygote cross of 3 yellow:1 white, but the observed ratio was 2:1. By performing test crosses, he determined that all the yellow mice were heterozygotes and that the yellow colour coat was the dominant phenotypic trait. However, no homozygous yellow mice were obtained. In 1910, William Ernest Castle and C. C. Little

reaffirmed Cuénot's discovery of a lethal gene by proving that a quarter of the offspring from crosses between heterozygotes died during embryonic development, due to failure to implant in the uterine lining. The quarter that died were the homozygous yellow mice that Cuénot did not see in his tests.

An example of lethal alleles in humans is achondroplasia,

a genetic condition which causes dwarfism. Affected

individuals are all heterozygotes, as the accumulation of

two mutant alleles is lethal and results in the ovum not

forming.

Another example of a lethal allele, this time in cats, is the Manx cat. Manx cats, if homozygotic, will not survive.

Heterozygotic Manx cats have characteristically short

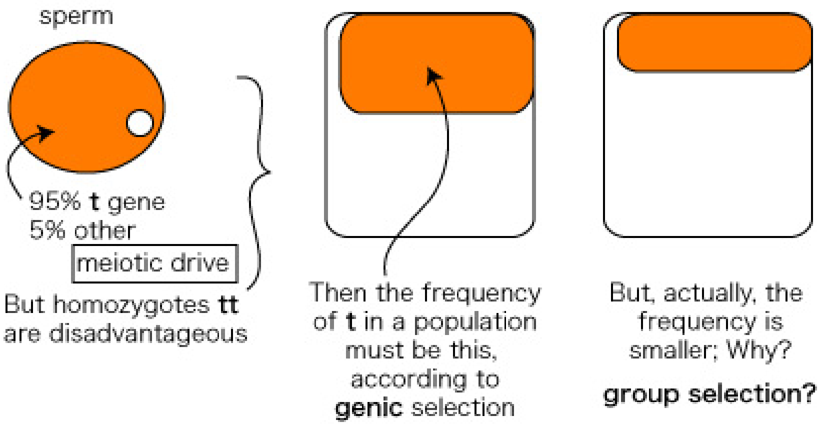
tails.

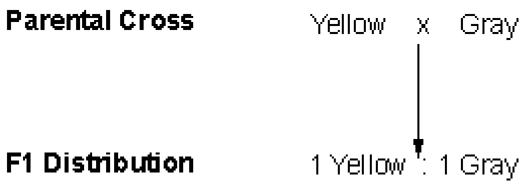
Figure: The yellow homozygote has a lethal phenotype

In case of **maize**, albinism is example of lethal factor.

The lethal factor in heterozygous condition has no lethal

effect but in homozygous condition it makes plant to die. Lethal factor in homozygous condition produces albino plant, which is unable to synthesize food due to lack of chlorophyll. Thus, the lethal factor modifies normal ratio from 3:1 to 2:1.


sperm
95% **t** gene
5% other
meiotic drive
But homozygotes **tt** are disadvantageous
Then the frequency of **t** in a population must be this, according to **genic** selection
But, actually, the frequency is smaller; Why?
group selection?



1.1.4 Meiotic Drive

Meiotic drive (also called segregation distortion) is any process which causes one gametic type to be over- or under-represented in the gametes formed during meiosis, and hence in the next generation.

A classic example of meiotic drive is the T locus in mice. This locus affects tail length and

viability. TT homozygotes have normal long tails; Tt heterozygotes have short tails and transmit ~

90% of the t allele to their sperm; tt homozygotes are sterile. Meiotic drive will increase frequency of the t allele to point where that become frequent enough to occur as tt homozygotes with appreciable frequency, whereupon selection works against t alleles. This shows two levels selection: positive selection for t haplotypes at the level of the gene, negative selection for tt individuals at the level of the genotype (organism).

The T locus (T/t complex) is indeed the best understood example of meiotic drive in mammals.

However, the phenotypes of the T locus as presented in the text above are wrong. T/T

homozygosity is embryonic lethal. Not only tail is missing but whole distal part of the body is disorganized. Tt mice are viable but have no tails. Tt males but not females transmit the t allele to 90% or more of their offspring. Finally, the tt homozygotes can be either lethal or viable. If viable, they can be either sterile (again only males) or fertile, all depending on the combination of particular t alleles (more properly t haplotypes)

1.1.5 Pleiotropism

During the first years after the rediscovery of Mendel's laws, a number of experiments were performed that gave results that at first glance did not coincide with the laws. In 1904, a cross was made between a yellow-coated mouse and a mouse with a gray coat.

The gray- coated mouse was extensively inbred and therefore was considered to be pure bred.

What allelic relationship do we have here? We know that the gray mouse is homozygous (because it is a pure line). If gray coat was dominant then we would see all gray mouse.

Since we obtain both yellow and gray mice, yellow must be dominant to gray. So what are the genotypes of the two mice populations? First, let's provide gene symbols.

Gene Symbols: gray = *y*

yellow = *Y*

From the above discussion, the genotype of the gray mouse must be *yy*. What is the genotype of the yellow mouse? If the mouse was homozygous we would not see any gray mice from the cross, therefore the genotype must be heterozygous or *Yy*.

Next a cross was made between two yellow mice. What genetic ratio would we expect to see? *Yy* x *Yy* should give a ratio of 3 yellow:1 gray. The result, though, was a ratio of 2

yellow to 1 gray mice. **How can this result be explained?** Let's first set up a Punnett Square.

Expected Punnett Square

Female Gametes

Y

y

YY

Yy

Y

Male

(yellow) (yellow)

Gametes *y*

Yy

yy

(yellow) (gray)

As we can see, we should get a 3:1 ratio of yellow to gray mice. Could some genotype be absent from the progeny. How can we test the genotypes of the yellow mice, since we already know the genotypes of the gray mice are *yy*. Testcross!! All testcross data with the yellow mice give a 1:1 ratio. This ratio is typical of what is seen with heterozygous individuals. Therefore, all of the yellow mice from the cross of two heterozygous yellow mice are genotypically *Yy*. Somehow the *YY* genotype is lethal. The 2:1 ratio is the typical ratio for a lethal gene.

Fig: **Coat Color in Mice**

Pleiotropic gene - a gene that affects more than one phenotype In this example the gene that causes yellowing of the coat also affects viability and is termed a pleiotropic gene.

1.1.6 Polygenic Inheritance

Polygenic inheritance is a pattern responsible for many features that seem simple on the surface. Many traits such as height, shape, weight, color, and metabolic rate are governed by the cumulative effects of many genes. Polygenic traits are not expressed as absolute or discrete characters, as was the case with Mendel's pea plant traits.

Instead, polygenic traits are recognizable by their expression as a gradation of small 9

M.Sc. Zoology I Sem: Paper-II: Genetics & Evolution differences (a continuous variation). The results form a bell shaped curve, with a mean value and extremes in either direction.

Example of Polygenic inheritance:

Human skin color is a good example of polygenic (multiple gene) inheritance. Assume that three "dominant" capital letter genes (A, B and C) control dark pigmentation because more melanin is produced. The "recessive"al eles of these three genes (a, b

& c) control light pigmentation because lower amounts of melanin are produced. The words dominant and recessive are placed in quotation marks because these pairs of alleles are not truly dominant and recessive as in some of the garden pea traits that Gregor Mendel studied. A genotype with all "dominant" capital genes (AABBCC) has the maximum amount of melanin and very dark skin. A genotype with all "recessive"

small case genes (aabbcc) has the lowest amount of melanin and very light skin. Each

"dominant" capital gene produces one unit of color, so that a wide range of intermediate skin colors are produced, depending on the number of "dominant"

capital genes in the genotype. For example, a genotype with three "dominant" capital genes and three smal case "recessive" genes (AaBbCc) has a medium amount of melanin and an intermediate skin color. This latter genotype would be characteristic of a mulatto.

In the following cross between two mulatto genotypes (AaBbCc x AaBbCc), each parent produces eight different types of gametes and these gametes combine with each other in 64 different ways resulting in a total of seven skin colors. The skin colors can be represented by the number of capital letters, ranging from zero (no capital letters) to six (all capital letters). The approximate shades of skin color corresponding to each genotype are shown in Table 1. Note: Skin color may involve at least four pairs of alleles with nine (or more) shades of skin color.

Gametes ABC ABc AbC Abc aBC aBc abC abc ABC

6

5

5

4

5

4

4

3

ABc

5

4

4

3

4

3

3

2

AbC

5

4

4

3

4

3

3

2

Abc

4

3

3

2

3

2

2

1

aBC

5

4

4

3

4

3

3

2

aBc

4

3

3

2

3

2

2

1

abC

4

3

3

2

3

2

2

1

abc

3

2

2

1

2

1

1

0

Table 1. Polygenic inheritance in people showing a cross between two mulatto parents (AaBbCc x AaBbCc). The offspring contain seven different shades of skin 10

M.Sc. Zoology I Sem: Paper-II: Genetics & Evolution color based on the number of capital letters in each genotype.

The cross in Table 1 can also be shown with the bionomial expansion (a + b)**6** where the letter a = number of capital letters and the letter b = number of small case letters.

Each term in the expression represents the number of offspring with a specific skin color phenotype based on the number of capital letters in the genotype. For example, 20 offspring have three capital letters in their genotype and have a skin color that is intermediate between very dark with all caps (AABBCC) and very light with no caps (aabbcc).

(a + b)6 = a6 + 6 a5b + 15 a4b2 + 20 a3b3 + 15 a2b4 + 6 ab5 + b6

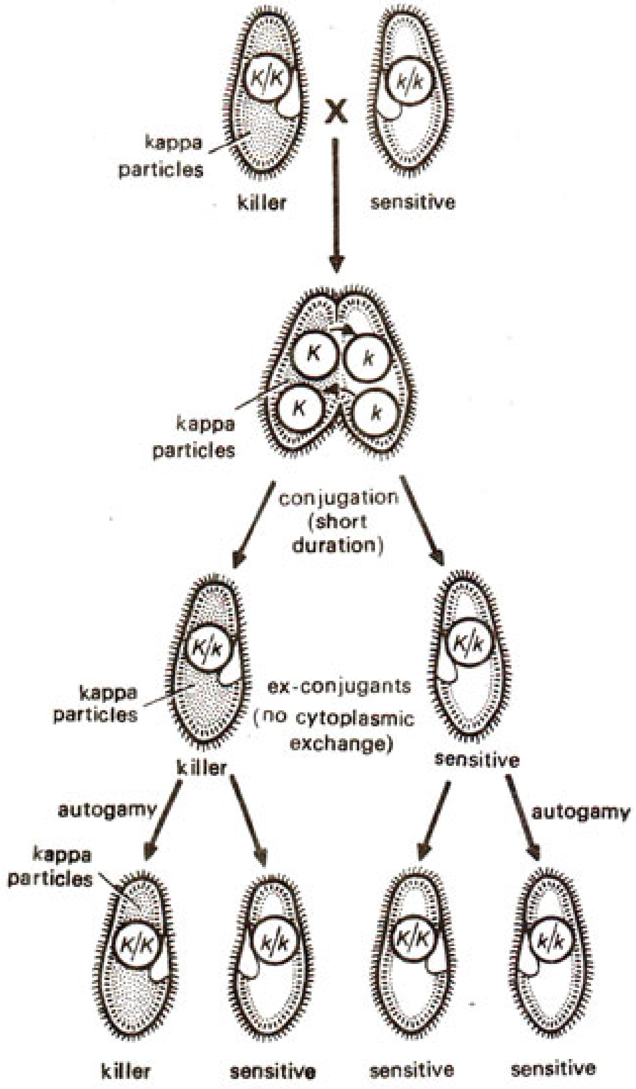
6 Caps 5 Caps

4 Caps

3 Caps

2 Caps

1 Cap 0 Caps



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1.1.7 Extra Chromosomal Inheritance:

Definition: Inheritance of traits through DNA that is not connected with the chromosomes but rather to DNA from organelles in the cell. Also called *cytoplasmic inheritance.*

Example: **Kappa particles in *Paramecium***

Kappa particles are found in certain killer strains of *Paramecium* and are responsible for production of substance **paramecin,** which is toxic to strains not possessing **kappa** (sensitive strain). The production of kappa particles is dependent on a dominant allele *K*, so that killer strains are *KK* or *Kk* and sensitive strains are ordinarily *kk.* In absence of dominant allele *K*, kappa particles cannot multiply and in absence of kappa particles, dominant allele *K* cannot produce them *de novo.* Consequently sensitive strains with genotypes *KK* or *kk* can be obtained. These will not carry any kappa particles. However, killer strain with genotype *kk* cannot be obtained, because even if kappa particles are present, these would be lost in absence of dominant allele. If *Paramecium* clones with genotypes *KK* or *Kk* are allowed to multiply asexually at such a fast rate, that division of kappa particles cannot keep pace with division of cells, kappa particles will be eventually lost. Consequently sensitive strains with dominant genotype (*KK*, *Kk*)having no kappa particles would be obtained.

If the killer (*KK*)and sensitive (*kk*)strains are allowed to conjugate, all exconjugants (the cells separating after conjugation) will have same genotype *Kk*. Phenotypes of these exconjugants will, however, depend upon duration for which conjugation is allowed. If conjugation does not persist long enough for exchange of cytoplasm, heterozygote (*Kk*)exconjugants will only have parental phenotypes. It means that killers will remain killers and sensitive will remain sensitive even after conjugation (Fig. 1). If conjugation persists, sensitive strain will receive kappa particles and will become killer, so that exconjugants will be killers having genotype *Kk* (Fig. 2)

Figure-1: Results of a cross between a killer (KK *) and a sensitive (* kk *)strain of* Paramecium, *when no cytoplasmic exchange is allowed.*

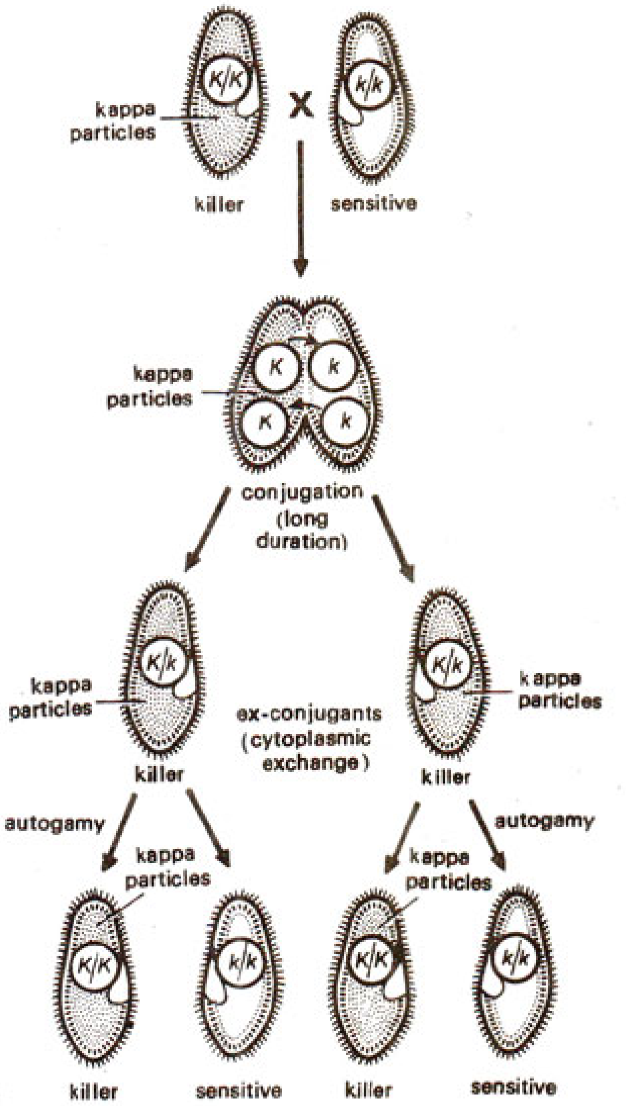
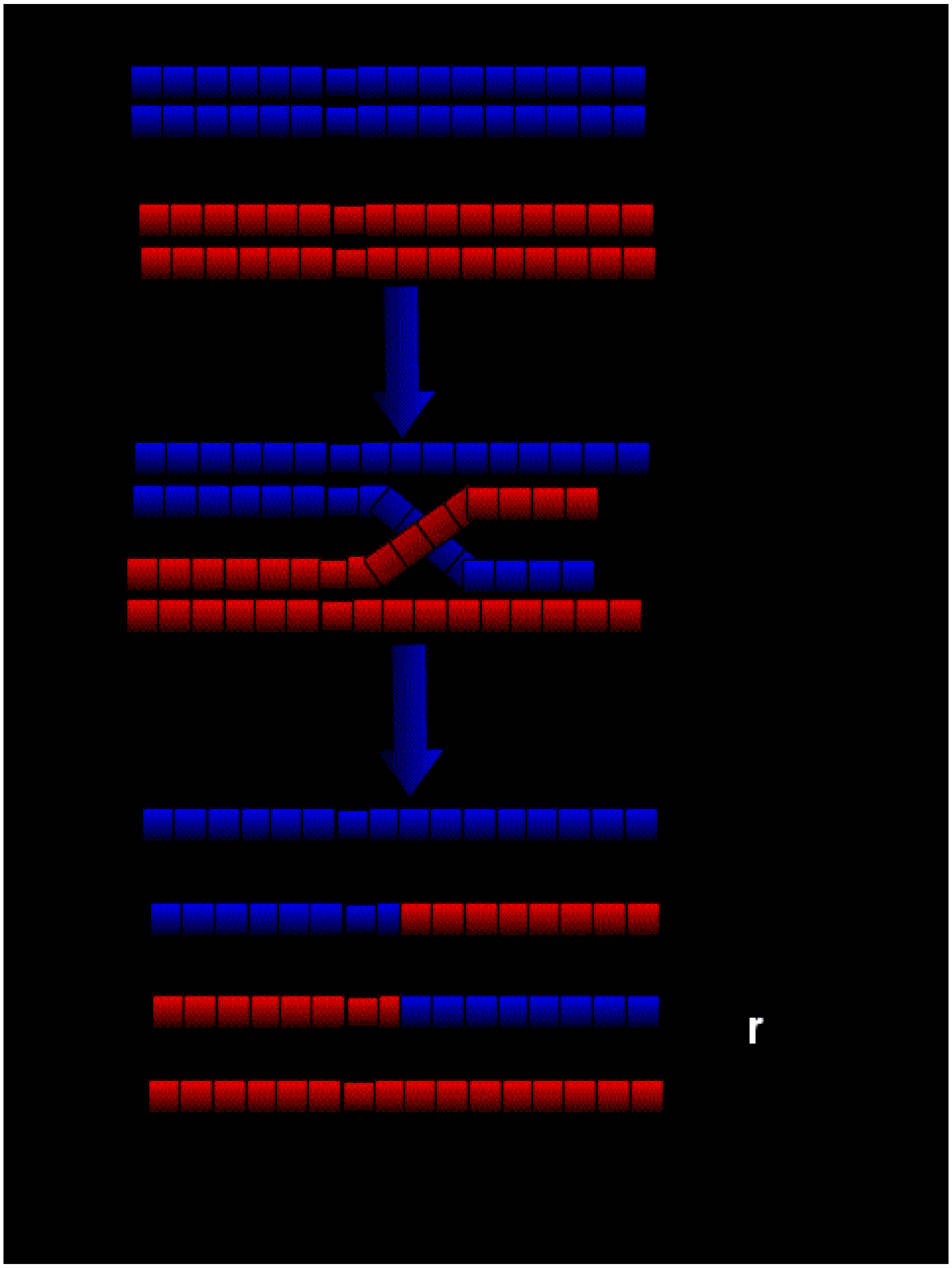


Figure-2 Results of a cross between a kiler (KK *)and a sensitive (* kk *)strain of* Paramecium, *when cytoplasmic exchange is allowed.*



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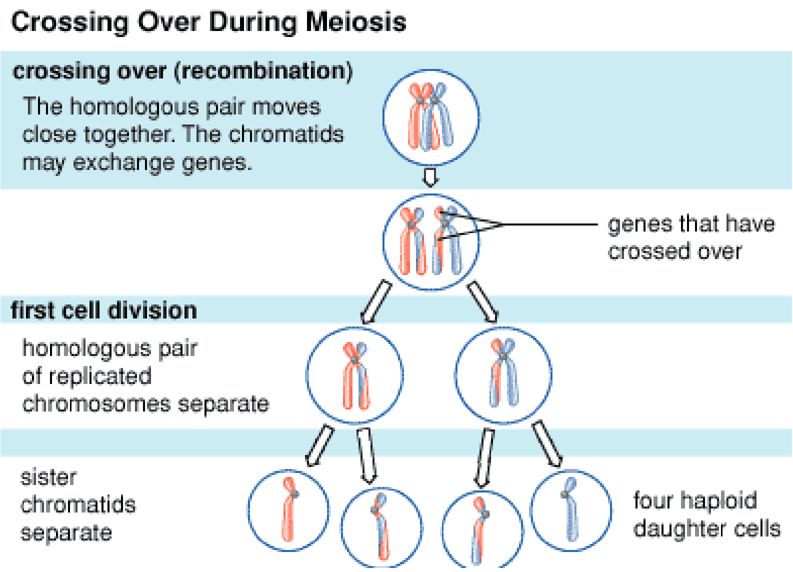
1.2 LINKAGE AND CROSSING OVER – COUPLING, TEST CROSS, LINKAGE MAPS, RECOMBINATION, CYTOLOGICAL BASIS FOR CROSSING-OVER

LINKAGE:

The tendency of genes located on the same chromosome to be found in the same gamete is called **linkage**. Linkage refers to a situation where two loci are on the same chromosome. Recall that if genes at two loci are on separate chromosomes, then they segregate independently. These loci are said to be uninked. This figure shows the tetrad during prophase 1 before crossing over takes place in a heterozygote with genotype AaBb, then shows one of many cross over events that could lead to new recombinants. Maternal chromosomes are shown in blue and paternal in red.

The next panel in this figure shows a cross over event that can lead to new chromosome types. These sorts of crossovers occur with frequency r where r is the frequency of recombination, while the third panel shows the four possible chromosomes after meiosis. and their frequencies. Generally the two chromosomes (1,4) are most common. These are often called the non recombinant or parental chromsomes because there has been no detectable crossing over between the loci during meiosis. This is because when sister chromatids swap segments, no recombination happens sunce sister chromatids start out prophase I with identical DNA. Chromosomes 2, 3 are recombinants which happen because of crossing over during meiosis.


Crossing Over During Meiosis
crossing over (recombination)
The homologous pair moves close together. The chromatids may exchange genes.
genes that have crossed over
first cell division
homologous pair of replicated chromosomes separate
sister chromatids separate
four haploid daughter cells

Importance of linkage

We are interested in linkage for two reasons:

• Linkage provides a way to map genes on chromosomes. Until modern gene mapping techniques linkage was the only way to do this. Even today linkage is important when used with other techniques to determine where on chromosomes certain genes are, especially for genes which have not been well studied and for understanding the mode of transmission for many genetic disorders.

• Linkage is also important in population genetics where the presence of linkage can vastly complicate the evolutionary behavior of genes in poulations.

CROSSING OVER/RECOMBINATION:

During meiosis, homologous chromosomes exchange some of their genes. This is called crossing over, or recombination. In most cases, crossing over is beneficial. It increases genetic variation, which in turn can introduce phenotypes that may give the individual a physical or even evolutionary advantage. It is one of the final phases of genetic

recombination, which occurs during prophase I of meiosis (pachytene) during a process called synapsis. Synapsis begins before the synaptonemal complex develops, and is not completed until near the end of prophase I. Crossover usually occurs when matching regions on matching chromosomes break and then reconnect to the other chromosome.

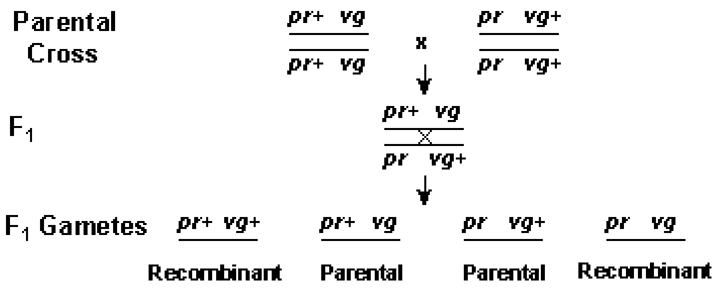
Crossing over was described, in theory, by Thomas Hunt Morgan. He relied on the discovery of the Belgian Professor Frans Alfons Janssens of the University of Leuven

who described the phenomenon in 1909 and had called it 'chiasmatypie'. The term

chiasma is linked if not identical to chromosomal crossover. Morgan immediately saw the great importance of Janssens' cytological interpretation of chiasmata to the experimental results of his research on the heredity of

Drosophila. The physical basis of crossing over was first demonstrated by Harriet Creighton and Barbara McClintock in 1931.

Crossing over occurs during meiosis I, and is the process where homologous chromosomes pair up with each other and exchange different segments of their genetic material to form recombinant chromosomes. It can also happen during mitotic division, which may result in loss of heterozygosity. Crossing over is essential for the normal segregation of chromosomes during meiosis. Crossing over also accounts for genetic variation, because due to the swapping of genetic material during crossing over, the chromatids held together by the centromere are no longer identical. So, when the chromosomes go on to meiosis II and separate, some of the daughter cells receive daughter chromosomes with recombined alleles. Due to this genetic recombination, the offspring have a different set of alleles and genes than their parents do.



COUPLING

The experiment was performed by Morgan when he crossed red eye, vestigal wing flies and purple eye, normal wing flies. Whereas in the first cross, the two dominant alleles and two recessive alleles were on the same chromosome the F1, in the is cross a dominant allele was on the same chromosome as a recessive allele. The term for the first chromosomal arrangement of the F1 is called **coupling**, whereas the second arrangement is called r**epulsion**. Another set of terms to describe these arrangements are **cis** and **trans**, respectively. The following shows the chromosomal arrangement for the cross of two parents in repulsion.

As with the first cross, Morgan testcrossed these F1 flies. The following table shows the distribution of these F1 gametes

F1 Gamete Testcross Distribution Gamete Type

pr+ vg+

157

Recombinant

pr+ vg

965

Parental

pr vg+

1067

Parental

pr vg

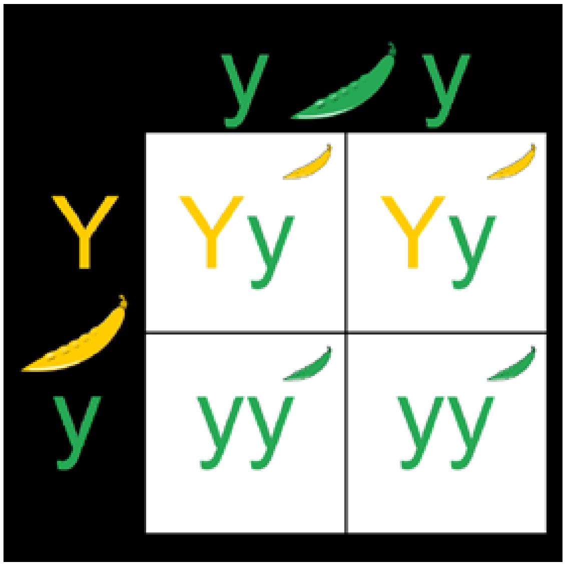
146

Recombinant

It was expected that both the coupling and repulsion crosses would yield 1:1:1:1

ratios. How can we determine if the results deviate from this ratio. As with any ratio, we can use the chi-square test to determine if the observed results fit or deviate from the expected ratio. The two tables below show the results for the chi-square for the two crosses.

It is quite clear that both of these large chi-square values indicate that neither of these ratios fit the 1:1:1:1



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Coupling Cross Chi-Square Test

F1 Gamete Observed Expected (O-E)2/E

pr+ vg+

1339

709.75 557.9

pr+ vg

151

709.75 439.9

pr vg+

154

709.75 435.2

pr vg

1195

709.75 331.8

Total

2839

2839

X2=1764.8

Repulsion Cross Chi-Square Test

F1 Gamete Observed Expected (O-E)2/E

pr+ vg+

157

583.75

312.0

pr+ vg

965

583.75

249.0

pr vg+

1067

583.75

483.3

pr vg

146

583.75

328.3

Total

2335

2335 X2=1372.6

TESTCROSS

In genetics, a **test cross**, first introduced by Gregor Mendel, involves the breeding of a

dominant trait individual with a recessive individual, in order to determine the

zygosity of the former by analysing proportions of offspring with the recessive

phenotype.

The genotype that an offspring has for each of its genes is determined by the allele inherited from its parents. The combination of alleles is a result of the maternal and paternal chromosomes contributed from each gamete at fertilization of that offspring.

During meiosis in gametes, homologous chromosomes

experience genetic recombination and segregate randomly into haploid daughter cells, each with a unique

combination of maternally and paternally coded genes.

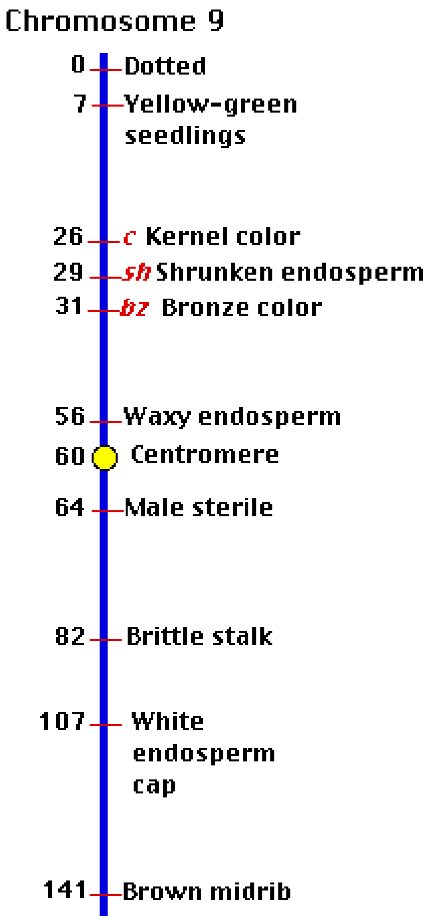
Fig: A Punnett square showing a typical test cross Test crosses involve breeding the individual in question

with another individual that expresses a recessive version of the same trait. If all offspring display the dominant phenotype, the individual in question is homozygous

dominant; if the offspring display both dominant and

recessive phenotypes, then the individual is heterozygous.

Diploid organisms, like humans, have two alleles at each genetic locus, or position, and one allele is inherited from each parent. Different alleles do not always produce equal outward effects or phenotypes. One allele can be dominant and mask the effect of a second recessive allele in a heterozygous organism that carries two different alleles at a specific locus. Recessive alleles only express their phenotype if an organism carries two identical copies of the recessive allele, meaning it is homozygous 17



for the recessive allele. This means that the genotype of an organism with a dominant phenotype may be either homozygous or heterozygous for the dominant allele.

Therefore, it is impossible to identify the genotype of an organism with a dominant trait by visually examining its phenotype.

To identify whether an organism exhibiting a dominant trait is homozygous or heterozygous for a specific allele, a scientist can perform a test cross. The organism in question is crossed with an organism that is homozygous for the recessive trait, and the offspring of the test cross are examined. If the test cross results in any recessive offspring, then the parent organism is heterozygous for the allele in question. If the test cross results in only phenotypically dominant offspring, then the parent organism is homozygous dominant for the allele in question.

LINKAGE MAPS

When all the members of the population have been scored (genotyped) with a set of molecular markers, the data can be used to make a linkage map (often described as a genetic map). The linkage map describes the linear order of markers within linkage groups.

This process estimates how the markers are grouped together based on the number of recombination breaks between them (recombination frequency) with one genetic map unit equal to the distance between marker pairs for which one product of meiosis out of a hundred is recombinant (recombination frequency of 1 per cent).

A mapping function (Haldane, Kosambi or Morgan) converts the recombination frequencies into mapping units, typically centimorgan units.

If we can resolve the genotype data into the same number of linkage groups as there are chromosomes we can use markers within groups that have previously been shown to map to a particular chromosome to order our linkage groups relative to their correct chromosomal assignments.

Example:

A genetic map of chromosome 9 (the one that carries

the **C**, **Sh**, and **bz** loci) of the corn plant (***Zea mays***) is shown on the right. If one maps in small intervals from one end of a chromosome to the other, the total number of centimorgans often exceeds 100 (as you can see for chromosome 9). However, even for widely-separated loci, the maximum frequency of recombinants that can form is 50%.

And this is also the frequency of recombinants that we see for genes independently assorting on separate chromosomes. So we cannot tell by simply counting recombinants whether a pair of gene loci is located far apart on the same chromosome or are on different chromosomes. As we saw above, several of Mendel's independently assorting traits are controlled by genes on the same chromosome but located so far apart that they are inherited as if they were located on different chromosomes.

Genes that are present on the same chromosome are called **syntenic**.

CYTOLOGICAL BASIS FOR CROSSING-OVER

Discussion in preceding sections of this section is based on the study of progeny in BC1

generation or the testcross progeny. In such progenies, lack of independent assortment demonstrated linkage and presence of recombinants showed crossing over. It was concluded that crossing over should be the result of exchange of chromosome segments. However, since homologous chromosomes normally exchange reciprocal segments, resulting chromosomes will exhibit no morphological differences. Therefore, except the visible chiasmata, there is no other cytological observation which will substantiate that actual exchange of chromosome segments really takes place.

However, it is not necessary that chiasmata should be associated with exchange of chromosome segments. Therefore, to demonstrate that crossing over is associated with actual exchange of chromosome segments, special experiments were devised by G.

Stern in *Drosophila* and by **H.S. Creighton** and **B. McCHntock** in corn. These experiments were reported in 1931 and had utilized chromosomes, whose morphology was altered due to chromosomal aberrations in order to make it identifiable from its homologue. Another experiment was conducted by M. Meselson and J. Weigle in lambda *(λ)* phage, demonstrating exchange of DNA segments.

Stern's experiment in *Drosophila*

Drosophila (fruitfly) stocks carrying translocations were utilised by **C. Stern** in order to produce a female *Drosophila* having a part of Y-chromosome attached to one of the two X-chromosomes. The **other** X-chromosome of this female fly was also marked (identifiable due to distinct morphology) and consisted of two approximately equal fragments, each carrying its centromere. These two X-chromosomes in the female fly could be distinguished not only from each other, but also from normal X-chromosome under the microscope.

In the above female fly, one of the two fragments of an X-chromosome carried mutant alleles for *carnation* eye *(car* is recessive showing light eye colour) and *barred* eye *(B* is dominant showing narrower eyes). The other X-chromosome, having a part of Y

attached, carried normal alleles of these two genes, so that the female heterozygote for both these genes *(car B/*+ +) had barred eyes (but normal eye colour, since *car* is recessive to +). Such females were crossed with male flies having recessive alleles for both these genes *(car,* +). In such a situation, this makes a simple testcross. If no crossing over takes place between the two genes in question, two types of gametes i.e., *car B* and ++ will be produced from the female flies. Crossing over will give two additional types ot gametes i.e., *car* + and + *B* (Figure 10.16). Due to fertilization of two types of non-crossover and the other two types of crossover gametes by male gametes carrying X-chromosome *(car* +), four kinds of female flies will be produced.

Another four kinds of male flies will be produced due to fertilization by Y carrying male gametes (Fig-1.).

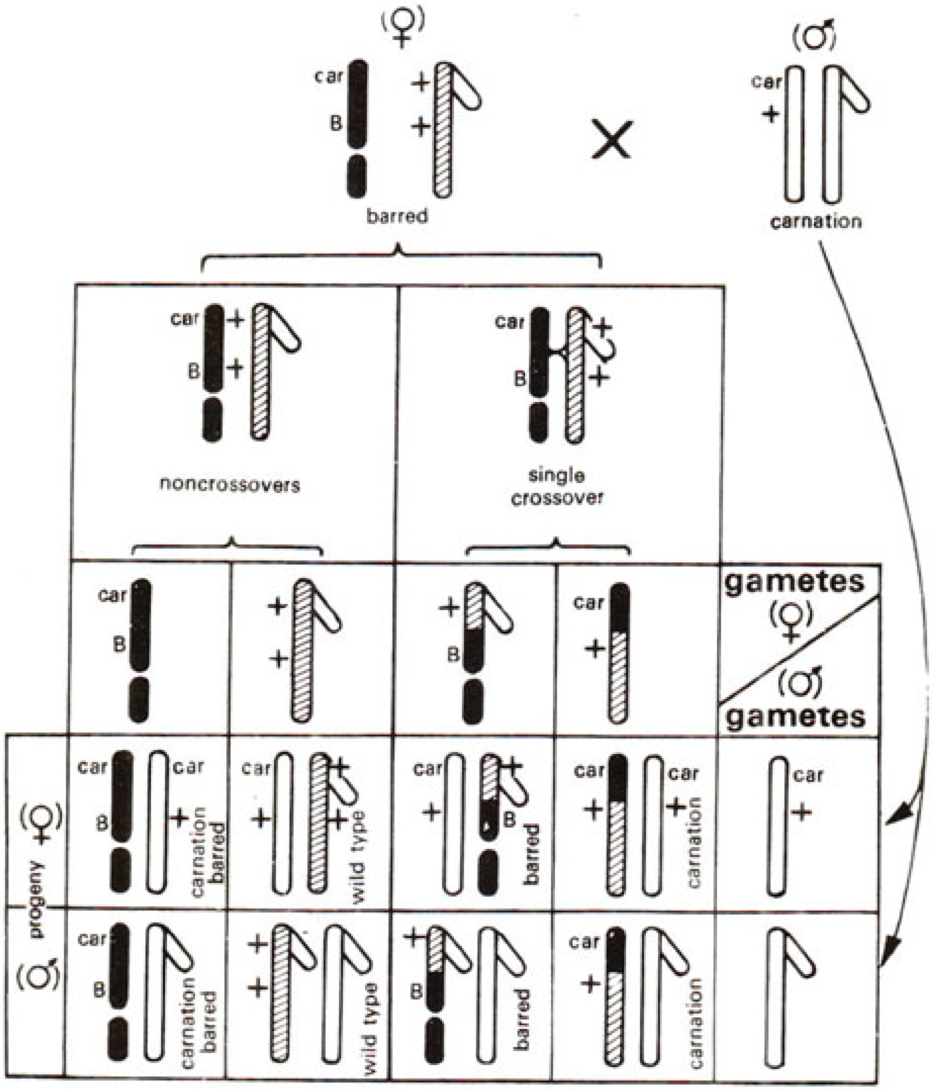


Fig.1. Stern's experiment to demonstrate cytological crossing over.

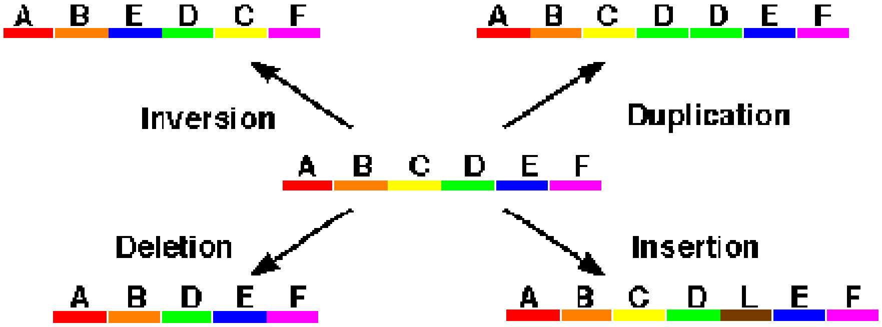
The flies which are classified as crossovers on the basis of phenotype i.e., carnation (with normal eye shape) and barred (with normal eye colour) were studied cytologically. It was found that carnation flies did not have any fragmented X-chromosome, but rather had normal X-chromosome. On the other hand, barred flies had a fragmented X-chromosome with a segment of Y-chromosome attached to one of the two fragments of X-chromosome. Such cytological observations suggested that genetic crossing over was accompanied with an actual exchange of chromosome segments.

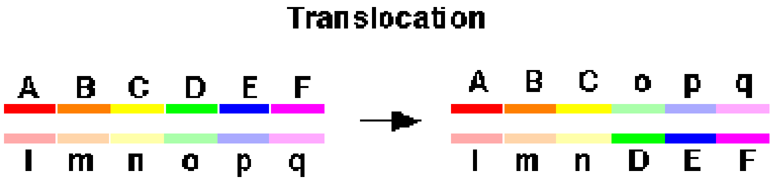
1.3 CHROMOSOMAL ABERRATIONS – STRUCTURAL AND NUMERICAL CHANGES

What is Chromosomal Aberrations:

Normally, humans have 23 pairs of chromosomes - making 46 in total. This includes one pair of chromosomes which are the sex chromosomes. The ova and the sperm each carry 23 chromosomes.

Chromosomal abnormalities occur when there is a defect in a chromosome, or in the arrangement of the genetic material on the chromosome. Very often, chromosome abnormalities give rise to specific physical symptoms, however, the severity of these can vary from individual to individual.





Abnormalities can be in the form of additional material which may be attached to a chromosome, or where part or a whole chromosome is missing, or even in defective formation of a chromosome. Any increases or decreases in chromosomal material interfere with normal development and function.

Chromosome aberrations are classified as one of two types: numerical or structural.

Numerical changes are to two types: polyploidy with changes in the number of sets of chromosomes (polyploidy) and aneuploidy with changes in the number of individual chromosomes (e.g., trisomies and monosomies). Structural changes involve the loss or gain of portions of chromosomes. The resulting patient may be said to have "partial monosomy" or "partial trisomy."

Structural Aberrations:

These occur due to a loss or genetic material, or a rearrangement in the location of the genetic material. They include: deletions, duplications, inversions, ring formations, and translocations.

Fig: Types of structural chromosome changes

- Deletions: A portion of the chromosome is missing or deleted. Known disorders include Wolf-Hirschhorn syndrome, which is caused by partial deletion of the short arm of chromosome 4; and Jacobsen syndrome, also called the terminal 11q deletion disorder.

- Duplications: A portion of the chromosome is duplicated, resulting in extra genetic material. Known disorders include Charcot-Marie-Tooth disease type 1A which may be caused by duplication of the gene encoding peripheral myelin protein 22 (PMP22) on chromosome 17.

- Translocations: When a portion of one chromosome is transferred to another chromosome. There are two main types of translocations. In a reciprocal translocation, segments from two different chromosomes have been exchanged.

In a Robertsonian translocation, an entire chromosome has attached to another at the centromere; these only occur with chromosomes 13, 14, 15, 21 and 22.

- Inversions: A portion of the chromosome has broken off, turned upside down and reattached, therefore the genetic material is inverted.

- Rings: A portion of a chromosome has broken off and formed a circle or ring.

This can happen with or without loss of genetic material.

- Isochromosome: Formed by the mirror image copy of a chromosome segment including the centromere.

Structural aberrations also include some disorders which are characterized by chromosomal instability and breakage. One example, is the creation of a fragile site on the X Chromosome - Fragile X syndrome. Boys are worse affected by this because they only have one X-Chromosome but even in girls, Fragile X syndrome can cause learning difficulties.

Most chromosome anomalies occur as an accident in the egg or sperm, and are therefore not inherited. The anomaly is present in every cell of the body.Some anomalies, however, can happen after conception, resulting in mosaicism (where some cells have the anomaly and some do not). Chromosome anomalies can be inherited from a parent or be "de novo". This is why chromosome studies are often performed on parents when a child is found to have an anomaly.

Examples of Structural Chromosome Abnormalities

KARYOTYPE

COMMENT

46,XY,t(5;10)(p13;q25) Balanced reciprocal translocation involving chromosomes 5

and 10

(break points indicated)

45,XX,t(13;14)(p11;q11) Centric fusion translocation of chromosomes 13 and 14.

A Robertsonian translocation normal carrier

46,XY,del(5)(p25)

Short arm deletion of 5, Cri du chat syndrome

46,XX,dup(2)(p13p22) Partial duplication of the short arm of chromosome 2

(p13p22)

46,X,i(Xq)

Isochromosome of Xq; Turner female

46,XY,r(3)(p26q29)

Ring chromosome 3 (p26q29)

46,XY,inv(11)(p15q14) Pericentric inversion of chromosome 11

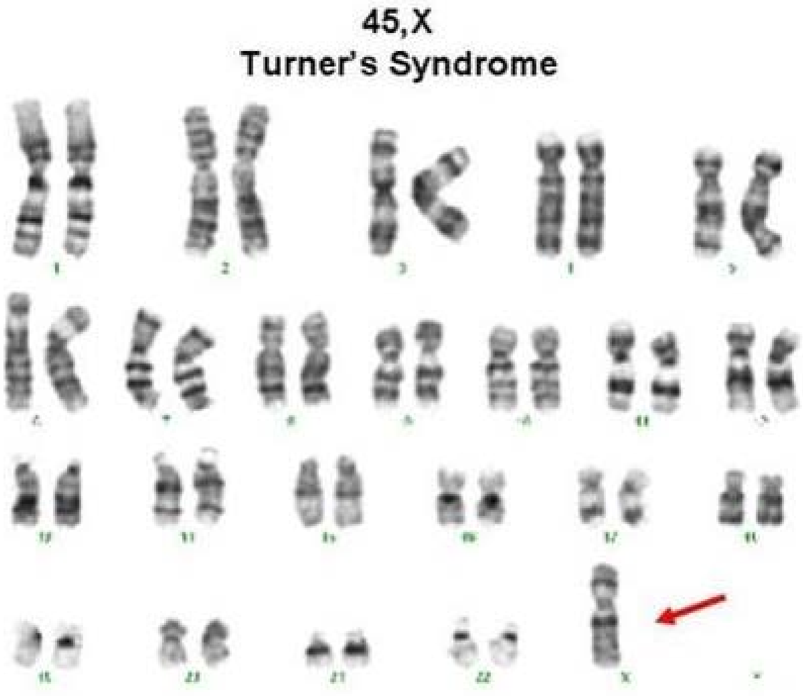
Numerical Aberrations:

This is called aneuploidy (an abnormal number of chromosomes), and occurs when an individual either is missing a chromosome from a pair (monosomy) or has more than two chromosomes of a pair (trisomy, tetrasomy, etc.).

In humans, an example of a condition caused by a numerical anomaly is Down

Syndrome, also known as Trisomy 21 (an individual with Down Syndrome has three copies of chromosome 21, rather than two). Trisomy has been determined to be a function of maternal age.

An example of monosomy is Turner syndrome, where the individual is born with only one sex chromosome, an X.



Turner Syndrome:

Turner syndrome (45,X) is the most frequent chromosomal abnormality. It is found in more than 7% of all spontaneous abortions. As it affects only about 1/2500 live female births, only about 2% of the recognized 45,X embryos survive to term, 98% are lost.

The nondisjunction that results in a 45,X female can occur at either meiotic division in either spermatogenesis or oogenesis, but about 80% are the result of paternal nondisjunction. Turner syndrome individuals can also result from early mitotic nondisjunction, being mosaic 46,XX/45,X.

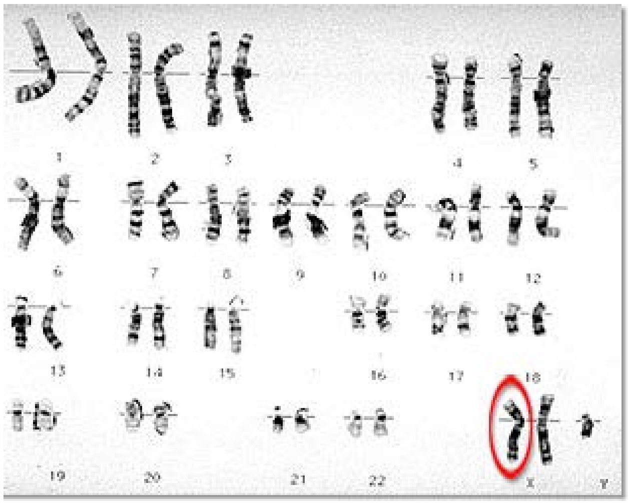
The phenotype of Turner syndrome individuals differs significantly from the normal female, even though the normal female has only one functioning X chromosome in each cell. The events of embryogenesis during the time both X chromosomes are functioning in the female must be critical, as well as those few regions of the X

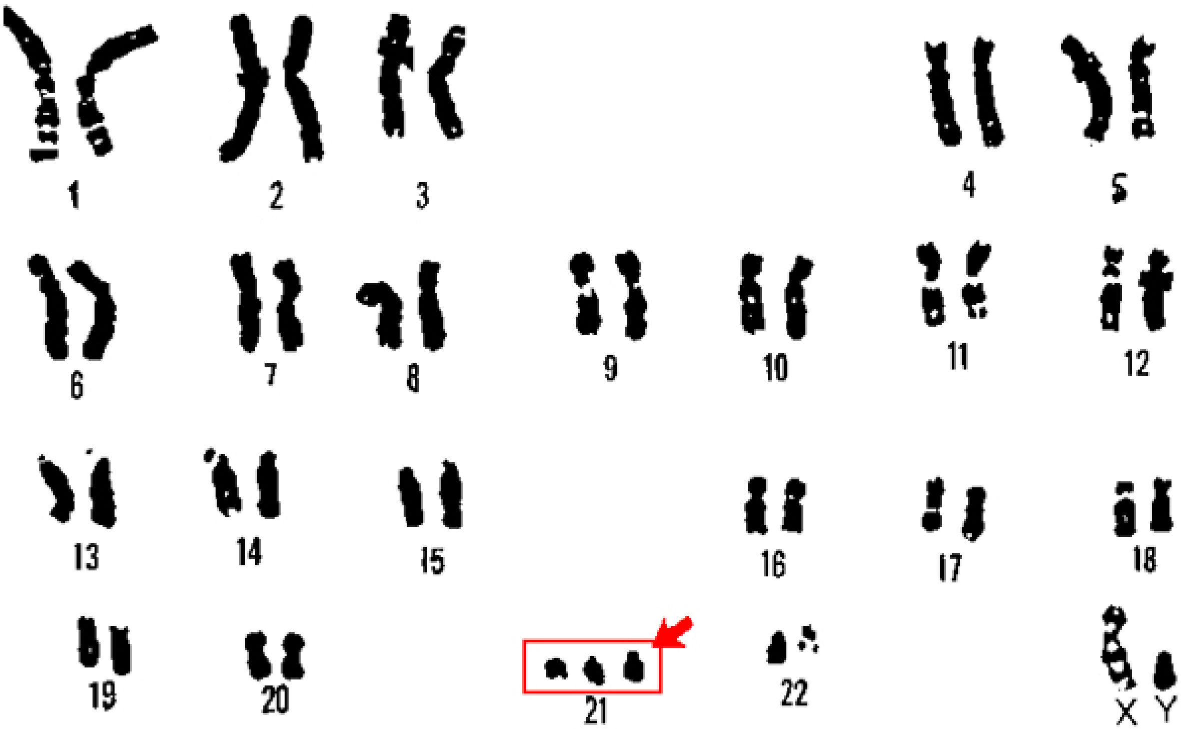
chromosome that are not inactivated.

Klinefelter Syndrome:

Klinefelter syndrome (47, XXY) occurs in about 1/850 male births. In the human, the presence of one Y chromosome produces male secondary sex characteristics in the absence of specific mutations for sex determining loci. Since the child must get his Y

chromosome from his father, the nondisjunction that produces a Klinefelter syndrome child could occur in either meiotic division of the mother, but could only occur in the first meiotic division in the father. If nondisjunction occurred in the father, the zygote would have to get both an X and a Y chromosome in the same sperm. In spermatogenesis this could only result from a mistake in first division. Second meiotic division of spermatogenesis separates either the two X chromatids into different gametes or the two Y chromatids into different gametes.





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Down Syndrome:

Down syndrome occurs in about 1 in 830 newborns. Most cases of Down syndrome result from trisomy 21, which means each cell in the body has three copies of chromosome 21 instead of the usual two copies.

Less commonly, Down syndrome occurs when part of chromosome 21 becomes attached (translocated) to another chromosome during the formation of reproductive cells (eggs and sperm) in a parent or very early in fetal development. Affected people have two normal copies of chromosome 21 plus extra material from chromosome 21

attached to another chromosome, resulting in three copies of genetic material from chromosome 21. Affected individuals with this genetic change are said to have translocation Down syndrome.

A very small percentage of people with Down syndrome have an extra copy of chromosome 21 in only some of the body's cells. In these people, the condition is called mosaic Down syndrome.

1.4 GENE MUTATIONS – IN DRASPHILA AND MAN

A gene mutation is a permanent change in the DNA sequence that makes up a gene.

Mutations range in size from a single DNA building block (DNA base) to a large segment of a chromosome.

Thomas Hunt Morgan described 61 mutations in his 1925 book, *The Genetics of Drosophila*. Mutations are changes in the chromosomes, genes, or part there of, resulting in a change in the characterists of an organism. Mutations caused by large changes in chromosome arrangement, such as inversions and deletions, can be observed under the microscope in the banding of a chromosome squash, and the position of breakpoints noted. Such chromosomal rearrangements often affect more than one gene.

Gene mutations occur in two ways: they can be inherited from a parent or acquired during a person’s lifetime. Mutations that are passed from parent to child are called hereditary mutations or germline mutations (because they are present in the egg and sperm cells, which are also called germ cells). This type of mutation is present throughout a person’s life in virtually every cell in the body.

Mutations that occur only in an egg or sperm cell, or those that occur just after fertilization, are called new (de novo) mutations. De novo mutations may explain genetic disorders in which an affected child has a mutation in every cell, but has no family history of the disorder.

Acquired (or somatic) mutations occur in the DNA of individual cells at some time during a person's life. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, or can occur if a mistake is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed on to the next generation.

Mutations may also occur in a single cell within an early embryo. As all the cells divide during growth and development, the individual will have some cells with the mutation and some cells without the genetic change. This situation is called mosaicism.

Some genetic changes are very rare; others are common in the population. Genetic changes that occur in more than 1 percent of the population are called polymorphisms.

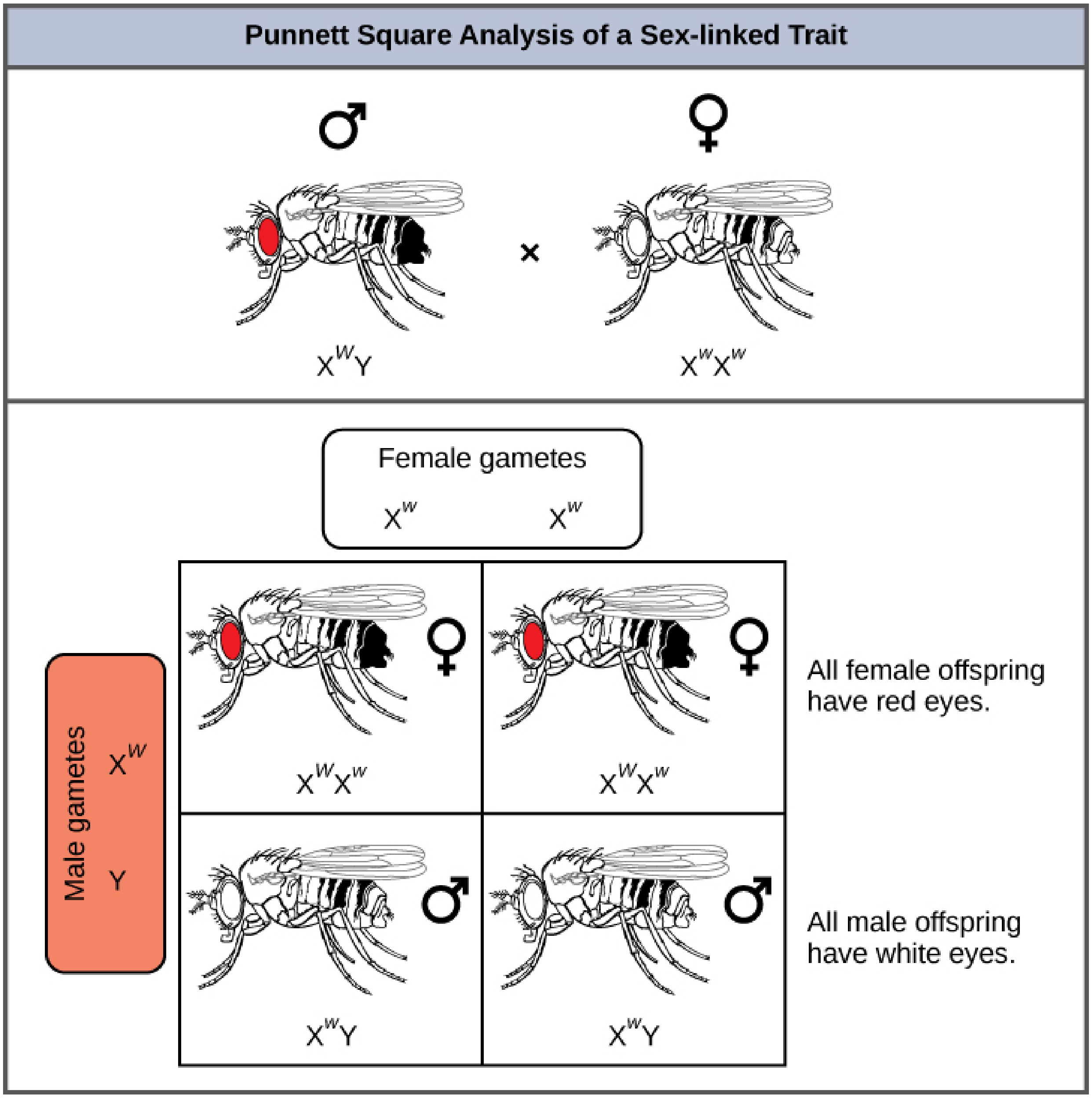
They are common enough to be considered a normal variation in the DNA.

Polymorphisms are responsible for many of the normal differences between people such as eye color, hair color, and blood type. Although many polymorphisms have no negative effects on a person's health, some of these variations may influence the risk of developing certain disorders.

Gene Mutations in Drasophila:

Drosophila melanogaster, or the red-eyed pomace fly, is classified in the family Drosophilidae, and order Diptera (which also includes flies, mosquitoes and midges.) Scientists study simple model systems in hopes of understanding principles that can apply to complex systems. *Drosophila* has been such a model organism for several reasons. They are small, easy to raise in the Lab, have a short life-cycle, have only 4

pair of chromosomes, and contain large polytene chromosomes. Polytene chromosomes, found in the salivary glands of organisms in the order, Diptera, are actually 1,000s of copies of each chromosome lined up in register. Areas of dark and 25


Punnett Square Analysis of a Sex-linked Trait
♂
♀
×
X^W Y
X^w X^w
Female gametes
X^w
X^w
Male gametes
X^W
Y
♀
♀
X^W X^w
X^W X^w
♂
♂
X^w Y
X^w Y
All female offspring have red eyes.
All male offspring have white eyes.

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light bands contain various concentrations of DNA and protein in the chromatin, and can be seen under a light microscope at a magnification of 450X. (Salivary glands are important for flies in the production of material to make the pupal case; this may account for the giant size polytene chromosomes.) Each band has been assigned a number.

Hunt Morgan began at his Lab at Columbia University in 1909, set the stage for his discovery of sex linkage in fruit flies. The genetic cross activity in this unit is based on these experiments. He found that there is a mutation which affects eye color, changing it from the normal wild type red found in nature, to unpigmented and therefore white eyes. When a white-eyed male was crossed with a wild type female, all the offspring were red-eyed. This would show red-eyes to be dominant over white.

When these red-eyed offspring were mated, the results followed a predictable 3:1 Mendelian ratio of red to white. But the interesting thing about these results were that all the white-eyed flies were males. Half of the males were red-eyed, and all of the females were red-eyed. Morgan realized that these results could be explained if the gene for red vs white eye color were located on the X chromosome. In this experiment the parent (P) females have two X chromosomes each with a dominant red-eyed gene (homozygous for this trait) Males have only one X, in this case carrying the white-eyed mutation, and no gene for eye color on the Y. (This is termed hemizygous because the male can only have one possible copy of a gene, since the Y carries none.) The first generation (F1) offspring would be females all be carrying a red-eyed gene, and would therefore be red-eyed. In the F2 generation, all females would be red-eyed because male gametes could only have the red-eyed gene. Males would have a 50/50 chance of being red or white-eyed because half of the female gametes carry a white-eyed gene.

A rather strange and interesting mutation is Antennapedia (Antp) located on chromosome 3 position 47.5. This mutation may cause death, but if the fly survives to adulthood, they may have an extra pair of legs where the antennae should be. In some cases wing tissue also develops in the eyes.

Gene Mutations in Man

Tay-Sach’s sickness could be a well-documented disorder caused by a base deletion within the factor secret writing for hexosaminidase. This protein is vital for removal of bound ototoxic chemicals that may build up within the brain. Tay-Sach’s causes mental and physical impairment and may be fatal. associate insertion in body fifteen causes a frame shift within the hexosaminidase factor.

Crohn’s Disease is caused by the addition of a cystosine base on body sixteen. The addition of this base doesn’t utterly eliminate the operate of the protein product.

However, it will scale back overall activity, therefore resulting in inflammatory intestine sickness.

There area unit variety of well-known strategies researchers use to sight mutations in genetic materials. very often it’s a matter of comparison associate unknown sample with a wild sort to find base variations. machine-driven Sanger sequencing is employed to spot single base polymorphisms or SNPs. A sample is isolated from genomic desoxyribonucleic acid and amplified by the enzyme Chain Reaction to supply use able copies of a specific region of the ordination. Humans and different species area unit heterozygous in order that they contain 2 copies of every factor. A mutation in one copy would be detected as a heterozygous wherever 2 bases occupy an equivalent position within the sample.

Document Outline

- Types of Gene Interactions
- Non-allelic gene interaction
- Inter-allelic
- The epistasis is in between two genes, that is at least a dihybrid and the phenotypes are less than 4.
  - (a) Dominant epistasis (12: 3: 1):
  - (b) Recessive epistasis (9:3:4):
  - (c) Duplicate recessive gene (9: 7):
  - (d) Duplicate genes with cumulative effect (9:6:1):
  - Example of Lethal Genes
- Structural Aberrations:
  - Examples of Structural Chromosome Abnormalities